REMARKS

Claim Amendments

Claims 1-8, 10-26, and 28-44 were under consideration in the instant application. Claims 1, 3-8, 10, 18-26, 28, 37, 40, 42, and 44 have been amended, and claims 45-47 have been added. Accordingly, claims 1-8, 10-26, and 28-47 will be under examination in the application upon entry of the claim amendments and additions presented herein. A "marked-up version" setting forth the claims as amended herein is attached hereto as Appendix A.

Support for the claim amendments can be found throughout the specification and claims as originally filed. In particular, support for the amendment to 1 and 18 can be found at least at page 33 of the specification. Support for the amendment to claim 3 can be found in the specification at least at page 9. Support for the amendment to claim 8 can be found in the specification at least at page 2, lines 25-35; support for claim 10 can be found in the specification at least at page 2, lines 6-9; support for claim 25 can be found in the specification at least at page 2, lines 25-35 and page 3, lines 27-30; support for claims 37 and 40 can be found in the specification at least at page 15, lines 16-36; and support for claims 42 and 44 can be found in the specification at least at page 15, lines 33-36. Support for new claims 45-47 can be found in the specification at least at page 8 and at least at page 9, lines 9-27. No new matter has been added.

Amendments to and/or addition of claims should in no way be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action or in any previous Office Actions, and were made solely to expedite prosecution of the above-identified application. Applicant reserves the option to prosecute the same claims as those originally filed, or similar claims, in the instant application or one or more or subsequent applications.

Claim Rejections – 35 U.S.C. §112

35 U.S.C. §112, First Paragraph

Claims 18-26, 28-37, 43 and 44 are rejected under 35 U.S.C. §112, first paragraph, because, according to the Examiner, the specification is "enabling for a method of treating a xenogeneic subject having spinal cord damage as observed in the hemi-sected animal model or having spinal cord damage as observed in the animal model of amyotrophic lateral sclerosis," but "does not reasonably provide enablement for a method of treating a xenogeneic subject having spinal cord damage resulting from the claim-designated neurodegenerative disorders per se, the claim-designated spinal cord injuries per se, or aging." The Examiner is further of the opinion that

> the specification is non-enabling for methods of treating any neurodegenerative disorder such as degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, amyotrophic lateral sclerosis, multiple sclerosis, syringomyelia, spinal tumors or metastasis, and spinal cord infections, or aging. The specification discloses a particular model system for spinal cord lesions, *i.e.*, a hemi-sected animal model, wherein pig spinal cord cells are transplanted into the region of the lesion, and a model system for amyotrophic lateral sclerosis. The specification, however, does not disclose a particular method of treating all of the claim-designated neurodegenerative diseases, spinal cord injuries or aging, per se, such that therapeutic effectiveness is achieved in mammals suffering from degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, multiple sclerosis, syringomyelia, spinal tumors or metastasis, and spinal cord infections, or aging.

Applicant respectfully traverses this rejection for at least the following reasons.

The pending claims pertain to compositions for transplantation into a mammalian xenogeneic subject comprising isolated spinal cord cells obtained from a pig, such that treatment of spinal cord damage that would benefit from survival and integration of the spinal cord cells is obtained upon transplantation into the subject. The pending claims also pertain to methods of treating a mammalian xenogeneic subject having spinal cord damage that would benefit from survival and integration of porcine spinal cord cells by administering to the subject a composition comprising isolated spinal cord cells obtained

from a pig, such that treatment of spinal cord damage is obtained upon administration of the composition to the subject.

Under 35 U.S.C. §112, first paragraph, the Examiner has the "initial burden of setting forth a reasonable explanation as to why the scope of protection provided by [claims 18-26, 28-37, 43 and 44] is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993). Specifically, in *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995), it was held that:

> *Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.*

Additionally, the court stated that in the absence of a reason to doubt the objective truth of the teachings contained in the specification, the methods of making and using the claimed invention must be taken as complying with the requirements of §112, first paragraph. The Examiner has not met this burden.

Applicant respectfully submits that the teachings in the specification enable the treatment of a variety of different types of deficits that would benefit from transplantation of fetal spinal cord cells. Furthermore, Applicant demonstrates ***both survival and integration of transplanted fetal porcine spinal cord cells***, upon transplantation into a transgenic subject. Thus, disorders that would benefit from survival and integration of transplanted fetal porcine spinal cord cells, such as those taught in the specification, or additional disorders known to one of ordinary skill in the art, would be treatable using the claimed compositions and methods.

Applicant further teaches various ways by which spinal cord cells can be administered to treat such disorders. For example, Applicant provides working examples in which spinal cord cells were administered via grafting Gelfoam saturated with porcine fetal spinal cord cells into an immobilized spinal cord (see working example 2). In that example, rats which received the transplanted cells demonstrated transplant-mediated reestablishment of host spinal tracts on the cellular level as determined by measuring supraspinal serotonergic (5-HT) innervation and axonal projections from the dorsal root

ganglia using calcitonin gene-related peptide (CGRP) as a marker. Other methods known to those of skill in the art can also be used to administer the claimed compositions.

Furthermore, behavioral data obtained from tests such as contact placing reflex, open field, inclined plane, beam walking, righting reflex, grasping reflex, and locomotor behavior, demonstrates the beneficial effects of the grafts at the ***functional anatomical level***. Applicant also teaches, e.g., in Example III, ***successful treatment*** of SOD mice (a model of ALS) by transplanting fetal porcine spinal cord cells into the ventral horn of the spinal cord. Thus, Applicant has demonstrated survival and integration of transplanted cells, has provided working examples of the treatment of two types of spinal cord damage by transplantation of fetal porcine spinal cord cells (i.e., damage due to physical trauma to the spinal cord and damage due to a progressive neurodegeneration disease). Applicant submits that the specification provides sufficient teaching to enable the treatment of various kinds of spinal cord damage that would benefit from the survival and integration of porcine spinal cord cells. It is Applicant's position that one of ordinary skill in the art would be able to treat the claimed disorders for treatment without undue experimentation, particularly given the working Examples presented in the specification.

The Examiner is further of the opinion that "the specification does not disclose where the spinal cord cells should be administered, whether the spinal cord cells are a heterogeneous or homogeneous population of cells, the amount of spinal cord cells to be administered, or the age of the cells to be administered, *i.e.*, the time during embryonic development in which the cells were isolated."

In contrast, Applicant teaches exemplary cell compositions and methods of administering such compositions. The spinal cord cells of the invention are described in the instant specification (see, e.g., least at page 8, lines 17-32) where Applicant teaches that spinal cord cells are porcine embryonic cells which are isolated from porcine fetuses which display the desired characteristics for transplantation. Applicant also points out that the claims as pending do not require that the compositions be homogeneous, in fact, in one embodiment, glial cells can be present. In addition, Applicant provides sufficient teaching to enable one of ordinary skill in the art to administer the claimed compositions. For example, cells can be administered by transplanting Gelfoam saturated with porcine fetal spinal cord cells into the spinal cord or by administering to one side of the spine at

lumbar level L1 in the ventral horn of the spinal cord (see e.g., page 13 line 19 to page 22, line 4 of the specification). Applicant provides exemplary numbers of cells to transplant. Armed with the teachings in the specification one of ordinary skill in the art could readily treat a variety of different disorders using the claimed compositions or methods.

In light of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of these 35 U.S.C. §112, first paragraph, rejections.

35 U.S.C. §112, Second Paragraph

Claims 8, 10-12, 25, 36, 37, and 42-44 are rejected under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Applicant submits that Applicant's amendments have rendered moot the following 35 U.S.C. §112, second paragraph rejections. The Examiner asserts that claims 8 and 25 are rendered vague and indefinite for the phrase "capable of". This rejection is believed to have been obviated by the amendment to claims 8 and 25 to replace the term "capable of stimulating" with "stimulates." The Examiner asserts that claim 10 is rendered vague and indefinite for the phrase "into the human" as "there is no human recited in claim 8." This rejection is believed to have been obviated by the amendment to claim 10 to replace the term "human" with "xenogeneic subject".

The Examiner asserts that claim 36 is rendered vague and indefinite for the phrase "wherein spinal cord damage is spinal cord injury". The Examiner is of the opinion that "it is unclear what the distinction is between "damage" and "injury". Clarification is requested." This rejection is respectfully traversed. Applicant respectfully directs the Examiner's attention to page 15, lines 16-36 of the specification where it is taught that spinal cord damage includes morphological and/or functional abnormality of a spinal cord cell or a population of spinal cord cells as a result of, for example, spinal cord injury, neurodegenerative disorders and/or aging. Thus, as defined in the specification, spinal cord injuries are embraced by the term spinal cord damage and may result from compression (*e.g.*, chronic compression), contusions (bruising), distraction (stretching),

solid core lesions caused by central core syndrome, and injuries which sever or partially sever the spinal cord.

In light of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of these 35 U.S.C. §112, second paragraph, rejections.

Claim Rejections – 35 U.S.C. §103(a)

Rejection of Claims 1-4, 17-21, 36, and 39-44 Under 35 U.S.C. § 103(a)

Claims 1-4, 17-21, 36, and 39-44 are rejected under 35 U.S.C. §103(a) as being unpatentable over Giovanini *et al.*, (1997), further in view of Galpern *et al.* (1996). The Examiner states that Giovanini *et al.* "teach a method of treating a mammalian xenogeneic subject having spinal cord damage by administering to the subject a composition comprising an isolated spinal cord cell obtained from a human fetus, such that treatment of spinal cord damage is obtained upon administration of the composition" while Galpern *et al.* teach "the lack of availability of human fetal tissue, the difficulties in storing human fetal tissue, and that a means for circumventing the limitations associated with human fetal neural transplantation by grafting fetal neuroblasts derived from a xenogeneic donor, such as a pig, which allows for the sterile harvesting of large quantities of pathogen-free tissue of the desired embryonic age, and the prior art teachings of using porcine neurons to reconstruct neuronal circuitries *in vivo*." The Examiner, in particular, alleges that there is motivation to combine the references to make the claimed invention obvious. Applicant respectfully traverses this rejection.

To establish a *prima facie* case of obviousness for the claimed invention, there must have been some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in the manner proposed by the Examiner. Second, there must have been a reasonable expectation of success at the time the invention was made. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. See M.P.E.P. 2143. The prior art must suggest "to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process" and "[b]oth the suggestion and the reasonable

expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Dow Chemical Co.* 837 F.2d 469. 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

The pending claims pertain to compositions for transplantation into a mammalian xenogeneic subject comprising isolated spinal cord cells obtained from a pig, such that treatment of spinal cord damage that would benefit from survival and integration of the spinal cord cells is obtained upon transplantation into the subject. The pending claims also pertain to methods of treating a mammalian xenogeneic subject having spinal cord damage that would benefit from survival and integration of porcine spinal cord cells by administering to the subject a composition comprising isolated spinal cord cells obtained from a pig, such that treatment of spinal cord damage is obtained upon administration of the composition to the subject.

Giovanini teaches the use of spinal cord cells from a ***human fetus*** to treat chronic contusion. This reference fails to teach or suggest the claimed compositions and methods. In fact, the Examiner admits, at page 7 of the Office Action, that "Giovanini *et al.* do not disclose that the spinal cord cell is obtained from a pig, or an embryonic pig at the claim-designated stage of differentiation." Thus, the reference fails to teach or suggest isolated ***porcine*** spinal cord cells as claimed by Applicant.

Galpern teaches the use of ***ventral mesencephalic*** (VM) tissue from pig brain for transplantation in the brain. The reference states that these dopaminergic neurons can be used to treat Parkinson's disease. This reference ***does not*** teach or suggest the claimed composition comprising isolated porcine ***spinal cord cells obtained from a pig*** as claimed by Applicant. The VM cells taught in this reference are ***specific to the brain*** and ***cannot be isolated from the spinal cord.***

It is Applicant's position that, at the time the invention was made, one of ordinary skill in the art would not have been motivated to combine the Giovanini and Galpern references in the manner suggested by the Examiner. The Examiner has failed to point to any teaching in the cited references which would impel one of ordinary skill in the art to make the claimed invention. The prior art must suggest "to those of ordinary skill in the art that they ***should*** make the claimed composition or device, or carry out the claimed process" and "[b]oth the suggestion and the reasonable expectation of success ***must be***

founded in the prior art, not in the applicant's disclosure (emphasis added)." *In re Dow Chemical Co.* 837 F.2d 469. 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Applicant respectfully asserts that the teachings of the Giovanini and Galpern references used ***different populations of cells to treat entirely different disease states***. The Giovanini reference disclosed ***human*** spinal cord cells only for treatment in an animal model of ***chronic contusion***, while Galpern disclosed the use of porcine ***VM*** cells for treatment in an animal model of ***Parkinson's disease***. Thus, there was no motivation to modify the teachings of the references to arrive at the claimed invention.

With regard to the necessary legal standard for combining references, Applicant refers to *Arkie Lures v. Larew Tackle*, 119 F.3d 953, (Fed. Cir. 1997). In Arkie Lures, the Larew invention was directed to a "salt-impregnated fishing lure." In that case, the CAFC overturned the district court's finding of obviousness. The CAFC agreed that "[t]he use of salty bait to catch fish was known,[and] plastisol lures were known." *Id* at page 956. However, the CAFC found that although the literature on "fishing lures is apparently quite extensive, but despite the long use of salty lures and plastic lures, no reference was cited that showed or suggested this combination." The CAFC continued that "[t]he evidence showed the complexity of the plastic fishing lure art. Those in the field of the invention viewed Larew's invention not as a simple concept of adding salty taste to a known lure, but as a complex combination requiring experience of fishing and fishing lures and the technology of plastics." Id at page 957. The court further stated that:

> No prior art showed or suggested the combination of a plastisol lure with salt, although the prior art was extensive as to the separate elements, and suggested including organic attractants in plastic lures. . . . The question is not whether salt "could be used," as the district court concluded, but whether it was obvious to do so in light of all the relevant factors. . . ***.It is insufficient to establish obviousness that the separate elements of the invention existed in the prior art, absent some teaching or suggestion, in the prior art, to combine the elements***. Indeed, the years of use of salty bait and of plastic lures, without combining their properties, weighs on the side of unobviousness of the combination (emphasis added).

Id at pages 957 and 958.

Similar to the situation in the *Arkie Lures* case, it is Applicant's position that despite the fact that the prior art contained the separate elements of transplantation of non-porcine spinal cord cells and transplantation of porcine non-spinal cord cells, these individual teachings are insufficient to establish the obviousness of the claimed invention absent some teaching or suggestion in the art to combine and modify the teachings of those references to arrive at the claimed invention.

In further support of their position, Applicant points to the recent CAFC decision in *In re Rouffet*, 149 F.3d 1350. 47 U.S.P.Q.2d (BNA), 1453 (Fed. Cir. 1998). Rouffet filed a patent application directed to technology to reduce signal transmission and receptor interruptions in the transmission signals from satellites. Rouffet taught changing the shape of the beam transmitted by the satellite's antenna to a fan-shaped beam. The Examiner rejected Rouffet's claims as unpatentable over U.S. patent number 5,199,672 (King) in view of U.S. Patent number 4,872,015 (Rosen) and a report titled "A Novel Non-Geostationary Staellite Communications System" (Ruddy). The CAFC found that:

> [although] the board did not err in finding that the combination of King, Rosen, and Ruddy contains all of the elements claimed in Rouffet's application. . .the Board reversibly erred in determining that one of skill in the art would have been motivated to combine these references in a manner that rendered the claimed invention obvious. Indeed, the Board did not identify any motivation to choose these references for combination.

Similarly, it is Appellant's position that the Examiner has failed to point to ***any*** motivation to modify the compositions and methods of the cited references, which are taught to be successful. In *Rouffet* the Court of Appeals continued:

> [b]ecause the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness. See In re Gorman, 933 F.2d 982, 986,

> 18 U.S.P.Q. 2D (BNA) 1885, 1888 (Fed Cir. 1991). Lacking a motivation to combine references, the Board did not show a proper prima facie case of obviousness. This court reverses the rejection over the combination of King, Rosen, and Ruddy.

In re Rouffet at [*17].

Since the Examiner has not pointed to any teaching or suggestion in the art that would impel the ordinarily skilled artisan to modify the cited art to arrive the compositions and methods claimed by Applicant, it is Applicant's position that the Examiner has used Applicant's invention as a blueprint to combine the references.

In addition, even if there was motivation to combine the references, which denies, there was no reasonable expectation of success that isolated porcine spinal cord cells would be successful in treatment of spinal cord damage.

Furthermore, with respect to claims 3, 4, 20, 21, 45, and 46-47 which claim specific gestational ages, percent viability, or percent of cells having neuron morphology, ***the combination of the cited references fails to teach or suggest all of the claim limitations***. Applicant has identified a population of isolated porcine spinal cord cells ideal for use in treatment of spinal cord disorders. This population of cells is isolated from fetal pigs between about 24 and about 30 days of gestation. The population of cells has characteristics which make them optimal for transplantation, e.g., they are at least about 50% viable and/or comprise about 30% cells having neural morphology. This population of cells is not taught or suggested in the cited art.

In view of the foregoing, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness in that there is no teaching or suggestion in any of the references relied upon by the Examiner, that would have motivated the ordinarily skilled artisan to arrive at Applicant's invention. Accordingly, Applicant respectfully requests that the rejection of claims 1-4, 17-21, 36, and 39-44 be reconsidered and withdrawn.

Rejection of Claims 1, 8, 10-12, 15, 16, 18, 25, 26, 28-31, 33, and 34 Under 35 U.S.C. § 103(a)

Claims 1, 8, 10-12, 15, 16, 18, 25, 26, 28-31, 33, and 34 are rejected under 35 U.S.C. §103(a) as being unpatentable over Giovanini *et al.* (1997), taken with Galpern *et al.* (1996), as applied to claims 1-4, 17-21, 36, and 39-44 above, and further in view of Chappel (1995). The Examiner relies on Giovanini *et al.* and Galpern *et al.* for the reasons set forth above. The Examiner is further of the opinion that

> [i]t would have been obvious for one of ordinary skill in the art at the time the claimed invention was made to obtain a composition of pig embryonic spinal cord cells at the appropriate stage of differentiation for the purpose of using the cells in a method of treating a mammalian xenogeneic subject suffering from spinal cord damage comprising administering the pig embryonic spinal cord cells to the subject. One of ordinary skill in the art would have been motivated to use pig as a source of cells for transplantation, for the reasons taught by Galpern *et al.* Moreover, one of ordinary skill in the art would have had a high expectation of successfully obtaining and using the cells in a method of treating spinal cord damage in view of the teachings of Giovanini *et al.* that administration of spinal cord cells to a xenogeneic mammal results in the claim-designated effect, *i.e.*, treatment of spinal cord damage. In addition, it would have further been obvious to mask the spinal cord cell with the anti-MHC class I F(ab')2 fragment of a monoclonal antibody, PT85, and to further provide a steroid such as methylprednisolone in the composition for administration in view of the teachings of Chappel that masking of the cell and providing methylprednisolone are means for reducing rejection of transplanted cells.

Applicant respectfully traverses the foregoing rejection on the basis that the Examiner has failed to establish a *prima facie* case of obviousness. Applicant respectfully submits that the primary references relied upon by the Examiner, namely the claims are not obvious over Giovanini *et al.* and Galpern *et al.*, for the reasons set forth above with respect to the 103(a) rejection of claims 1-4, 17-21, 36, and 39-44.

Moreover, the secondary reference of Chappel *et al.* does not make up for the deficiencies in the primary references. The teachings of Chappel *et al.* are limited to the use of pancreatic islet, liver, neural, muscle, and hematopoietic cells. Chappel *et al.* teaches masking of two or more epitopes on cells to reduce immunogenicity during transplantation. Chappel *et al.* does not teach or suggest the specifically claimed

compositions comprising an isolated spinal cord cell obtained from a pig for use in treating ***spinal cord damage***, as required by the pending claims.

Moreover, it is Applicant's position that there is no motivation to combine the references in the manner proposed by the Examiner. The Examiner has failed to point to any teaching in the cited references which would impel one of ordinary skill in the art to make the claimed invention. The prior art must suggest "to those of ordinary skill in the art that they ***should*** make the claimed composition or device, or carry out the claimed process" and "[b]oth the suggestion and the reasonable expectation of success ***must be founded in the prior art, not in the applicant's disclosure*** (emphasis added)." *In re Dow Chemical Co.* 837 F.2d 469. 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

In view of the foregoing, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness in that there is no teaching or suggestion in any of the references relied upon by the Examiner, that would have motivated the ordinarily skilled artisan to arrive at Applicant's invention. Accordingly, Applicant respectfully requests that this section 103(a) rejection be reconsidered and withdrawn.

Rejection of Claims 1, 5-7, 13, 14, 18, 22-24, 31, 32, 35, 37, and 38 Under 35 U.S.C. § 103(a)

Claims 1, 5-7, 13, 14, 18, 22-24, 31, 32, 35, 37, and 38 are rejected under 35 U.S.C. §103(a) as being unpatentable over Giovanini *et al.* (1997), taken with Galpern *et al.* (1996) as applied to claims 1-4, 17-21, 36, and 39-44 above, and further in view of Fraser (1996), Rosenbluth *et al.* (1997), and Wang *et al.* (1995). The Examiner relies on Giovanini *et al.* and Galpern *et al.* for the reasons set forth above. The Examiner is further of the opinion that

> Fraser *et al.* teach isolation of porcine neural cells, which by definition, includes both nerve cells, *i.e.*, neurons, and their precursors and glial cells, *e.g.*, oligodendrocytes and astrocytes, and their precursors (see, *e.g.*, page 10, lines 7-11). The neural cells can be obtained from any location in the pig central nervous system (see, *e.g.*, page 10, line 28-29). It is well known in the art that the spinal cord is part of the central nervous system. Although Fraser *et al.* do not specifically teach administering oligodendrocytes or astrocytes to damaged spinal cord areas, Rosenbluth

> *et al.* teach treating spinal cord injured xenogeneic mammalian subjects comprising administering oligodendrocytes (see, *e.g.*, page 173, under "Materials and Methods", and page 173-176, under "Results") and Wang *et al.* teach treating spinal cord injured xenogeneic mammalian subjects comprising administering astrocytes (see, *e.g.*, page 974, left column, and page 976-979, under "Results"). Thus, it would have been obvious to administer oligodendrocytes or astrocytes to spinal cord injured xenogeneic mammalian subjects in a method of treating spinal cord injury.

Applicant respectfully traverses the foregoing rejection on the basis that the Examiner has failed to establish a *prima facie* case of obviousness. Applicant respectfully submits that the primary references relied upon by the Examiner, namely that the claims are not obvious over Giovanini *et al.* and Galpern *et al* for the reasons set forth above with respect to the previous 103(a) rejections.

Moreover, the secondary references of Fraser, Rosenbluth *et al.*, and Wang *et al.* do not make up for the deficiencies in the primary references in that Fraser, Rosenbluth *et al.*, and Wang *et al.* do not teach or suggest Applicant's claimed compositions or methods, nor do the secondary references provide the motivation necessary to modify the teachings of the primary references. Fraser at al. do not specifically teach of suggest compositions comprising ***isolated spinal cord cell*** to treat ***spinal cord damage***, as required by the pending claims. The reference focuses on the use of ventral mesencephalic cells and does not provide motivation to use cells from the specific region claimed. Rosenbluth *et al.* teaches transplantation of glial cells obtained from the ***brains*** of ***embryonic mice*** (E16-E20), or ***neonatal mice*** (P1-2) into spinal cords of immunosuppressed rats in order to repair demyelination, not compositions comprising an ***isolated porcine spinal cord cell*** to treat spinal cord damage, as claimed by Applicant. Thus, the reference teaches cells from a different region and from a different animal. Wang *et al.* teaches implantation of neonatal ***rat cortical astrocytes*** into hemisected adult rat spinal cords, not compositions comprising an ***isolated porcine spinal cord cell***, as required by the pending claims. Thus, similar to Rosenbluth, the cells taught by this reference are from a different animal and are derived from a different site in that animal.

Because of these differences between the teachings in the art and the claimed invention, it is Applicant's position that there is no motivation to combine the references in the manner proposed by the Examiner. The Examiner has failed to point to any

teaching in the cited references which would impel one of ordinary skill in the art to make the claimed invention. As set forth above, the prior art must suggest "to those of ordinary skill in the art that they ***should*** make the claimed composition or device, or carry out the claimed process" and "[b]oth the suggestion and the reasonable expectation of success ***must be founded in the prior art, not in the applicant's disclosure*** (emphasis added)." *In re Dow Chemical Co.* 837 F.2d 469. 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988). None of the secondary references such motivation. In addition, as set forth above, at the time the invention was made, there was no reasonable expectation of success in making the claimed invention.

In view of the foregoing, Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness in that there is no teaching or suggestion in any of the references relied upon by the Examiner, that would have motivated the ordinarily skilled artisan to arrive at Applicant's invention. Accordingly, Applicant respectfully requests that this section 103(a) rejection be reconsidered and withdrawn.

CONCLUSION

Reconsideration and allowance of the claims is respectfully requested. If a telephone conversation with Applicant's attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

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Dated: April 18, 2001

Appendix A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 1, 3-8, 10, 18-26, 28, 37, 40, 42, and 44 have been amended as follows:

1. (Amended) A composition for transplantation into a mammalian xenogeneic subject comprising ~~an~~ isolated spinal cord ~~cell~~ cells obtained from a pig, such that treatment of spinal cord damage that would benefit from survival and integration of the spinal cord cells is obtained upon transplantation into the subject.

3. (Amended) The composition of claim 2, wherein the spinal cord cells ~~is~~ are isolated from an embryonic pig between about days ~~20~~ 24 to 30 of gestation.

4. (Amended) The composition of claim 3, wherein the spinal cord cells ~~is~~ are isolated from an embryonic pig between about days 25 to 29 of gestation.

5. (Amended) The composition of claim 1, wherein the spinal cord cells ~~is an~~ are oligodendrocytes.

6. (Amended) The composition of claim 1, wherein the spinal cord cells ~~is an~~ are astrocytes.

7. (Amended) The composition of claim 1, wherein the spinal cord cells ~~is an~~ are neurons.

8. (Twice Amended) The composition of claim 1, wherein the cells, in unmodified form, ~~has~~ have an MHC class I antigen on the cell surface which ~~is capable of stimulating~~ stimulates an immune response against the cell in a xenogeneic subject, wherein the MHC class I antigen on the cell surface is altered to inhibit rejection of the cells upon introduction of the composition into the subject.

10. (Twice Amended) The composition of claim 8, wherein the cell ~~is~~ are contacted prior to transplantation into the ~~human~~ xenogeneic subject with at least one anti-MHC class I antibody or fragment thereof, which binds to the MHC class I antigen on the cell surface but does not activate complement or induce lysis of the cells.

18. (Amended) A method of treating a mammalian xenogeneic subject having spinal cord damage that would benefit from survival and integration of porcine spinal cord cells by administering to the subject a composition comprising ~~an~~ isolated spinal cord ~~cell~~ cells obtained from a pig, such that treatment of spinal cord damage is obtained upon administration of the composition to the subject.

19. (Amended) The method of claim 18, wherein the spinal cord cells are ~~is~~ obtained from an embryonic pig.

20. (Amended) The method of claim 19, wherein the spinal cord cells are ~~is~~ isolated from an embryonic pig between about days ~~20~~ 24 to 30 of gestation.

21. (Amended) The method of claim 20, wherein the spinal cord cells are ~~is~~ isolated from an embryonic pig between about days 25 to 29 of gestation.

22. (Amended) The method of claim 18, wherein the spinal cord cells are ~~is an~~ oligodendrocytes.

23. (Amended) The method of claim 18, wherein the spinal cord cells are ~~is an~~ astrocytes.

24. (Amended) The method of claim 18, wherein the spinal cord cells are ~~is an~~ neurons.

25. (Twice Amended) The method of claim 18, wherein the cells, in unmodified form, have ~~has~~ at least one MHC class I antigen on the cell surface which ~~is capable of stimulating~~ stimulates an immune response against the cells in the subject, wherein the MHC class I antigen on the cell surface is altered to inhibit rejection of the cells when introduced into the subject.

26. (Amended) The method of claim 25, wherein the cells are ~~is~~ contacted prior to introduction into the subject with at least one molecule which binds to at least one

antigen on the cell surface which antigen is capable of stimulating an immune response against the cells in the subject to alter the antigen on the cell surface to inhibit rejection of the cells when introduced into the subject.

28. (Amended) The method of claim 26, wherein the cells are ~~is~~ contacted prior to introduction into the subject with at least one anti-MHC class I antibody or fragment thereof, which binds to the MHC class I antigen on the cell surface but does not activate complement or induce lysis of the cells.

37. (Amended) The method of claim 35, wherein the spinal cord damage is a result of a neurodegenerative disorder.

40. (Amended) The composition of claim 1, wherein said spinal cord damage ~~is selected from~~ results from a condition selected from the group consisting of: spinal cord injury, neurodegenerative disorder, and aging.

42. (Amended) The composition of claim 40, wherein said neurodegenerative disorder is selected from the group consisting of degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, ~~spinal cord injury,~~ amyotrophic lateral sclerosis, multiple sclerosis, syringomyelia, spinal tumors or metastasis, bacterial spinal cord infections, and parasitic spinal cord infections ~~(e.g., parasitic or bacterial infections)~~.

44. (Amended) The method of claim 37, wherein said neurodegenerative disorder is selected from the group consisting of degeneration of cells in the spinal cord, physical deterioration, death of spinal cord cells, abnormal pattern of spinal cord cells, ~~spinal cord injury,~~ amyotrophic lateral sclerosis, multiple sclerosis, syringomyelia, spinal tumors or metastasis, bacterial spinal cord infections, and parasitic spinal cord infections ~~(e.g., parasitic or bacterial infections)~~.